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10/629,895	07/30/2003	John J. Rossi	1954-413	8585

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EXAMINER	
WHITEMAN, BRIAN A	

ART UNIT	PAPER NUMBER
1635	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

PTO-PAT-Email@rfem.com

Office Action Summary	Application No.	Applicant(s)	
	10/629,895	ROSSI ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3,5,6 and 11-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,5,6,11-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Objections

Claims 2 and 3 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 1 is directed to inserting a nucleic acid sequence into the adenoviral VA1 coding sequence however, claims 2 and 3 are directed to inserting the nucleic acid sequence into the promoter region of the adenoviral VA 1 sequence that is before the VA1 coding sequence.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 2, and 11-16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Agami et al. (US 7,241,618) taken with Doglio et al. (US 5,837,503) in further view of either Yu (AH) or Ambros (Cell, 2001, 107:823-6).

Agami et al. teach making and using an expression cassette comprising an adenoviral VA1 promoter operably linked to an siRNA molecule, wherein the siRNA molecule can be shRNA (columns 50-51 and Figures 8 and 10 and claim 3). Agami et al. teach that siRNA is a substrate for mammalian Dicer (columns 1-3). However, Agami does not specifically teach using RNAi in the vector, wherein the RNAi is precursor miRNA. In addition, Agami does not specifically teach the structural limitations of the VA1 promoter set forth in claims 1 and 2.

However, at the time the invention was made, Doglio et al. teach an expression cassette comprising an oligonucleotide has been inserted between or outside the boxes A and B constituting the promoter of said VA gene or into VA1 gene (columns 8, 10-15, and 19-22).

Furthermore, at the time the invention was made, Yu teaches an RNA polymerase III vector comprising shRNA can inhibit expression in mammalian cells. Also microRNA was well known to one of ordinary skill in the art as exemplified by Ambros (pages 823-826). Ambros teaches, "Animal genomes contain an abundance of small genes that produce regulatory RNAs of about 22 nucleotides in length (abstract)." "These microRNAs are diverse in sequence and expression patterns, and are evolutionary widespread, suggesting they may participate in a wide range of genetic regulatory pathways (abstract)."

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Agami taken with Doglio in further view of Yu and Ambros, namely to produce an expression cassette comprising an adenoviral VA1 promoter, wherein an RNAi molecule is contained within a non-essential stem region of the promoter or coding region of the VA1 gene. One of ordinary skill in the art would have been motivated to combine the teaching to avoid reducing the activity of the promoter or to successfully express the RNAi molecule in cells. "The combination of familiar elements according to known methods is likely to be obvious when it does no more than yield predictable results." See ***KSR v. Teleflex***, 550 U.S. ___, 127 S. Ct. 1727 (2007).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Agami taken with Doglio in further view of either Yu or Ambros, namely to produce a mammalian cell comprising the expression cassette comprising an adenoviral VA1 promoter, wherein an RNAi

molecule is contained within a non-essential stem region of the promoter or coding region of the VA1 gene. One of ordinary skill in the art would have been motivated to combine the teaching to avoid reducing the activity of the promoter. See ***KSR v. Teleflex***, Id.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Applicant's arguments filed 10/20/08 have been fully considered but they are not persuasive.

In response to applicant's argument that there is no motivation in the cited art to make such a substitution in the art for a skilled artisan to reasonable expect that the shRNA inserted into the VA1 transcript would be cleaved out, thus making it a substrate for Dicer, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer when expressed in cells as taught by Agami and Sharp.

In response to applicant's argument that Rossi teaches away from the presently claimed subject matter (ribozyme or antisense inserted into VA1 region are not processed out of the VA1 transcript which shRNA must be processed out of the VA1 transcript and cleaved by Dicer in order to be active) and provides no motivation to make the combination proposed by the examiner in view of the specific teaching away,

the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer when expressed in cells as taught by Agami.

Claims 1, 2, and 3 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Agami taken with Doglio in further view of either Yu or Ambros, as applied to claims 1, 2, and 11-16 above, and in further view of Cagnon et al. (AD).

Agami, Yu or Ambros taken with Doglio do not specifically teach the structural limitations of the VA1 promoter set forth in claim 3.

However, at the time the invention was made, Cagnon teaches inserting an RNAi molecule into a VA 1 expression cassette using a filled-in Not1 site that was ligated into the BstEII cleaved, filled in vector (page 252).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Agami taken with Yu, Ambros and Doglio in further view of Cagnon, namely to produce the expression cassette wherein the non-essential stem region contains a BstEII site. One of ordinary skill in the art would have been motivated to combine the teaching to clone the siRNA into the VA1 promoter of the expression cassette since the restriction site is found in an adenoviral VA1 promoter. See KSR v. Teleflex, Id.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In response to applicant's argument that there is no motivation in the cited art to make such a substitution in the art for a skilled artisan to reasonable expect that the shRNA inserted into the VA1 transcript would be cleaved out, thus making it a substrate for Dicer, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer when expressed in cells as taught by Agami and Sharp.

In response to applicant's argument that Rossi and Cagnon teach away from the presently claimed subject matter (ribozyme or antisense inserted into VA1 region are not processed out of the VA1 transcript which shRNA must be processed out of the VA1 transcript and cleaved by Dicer in order to be active) and provides no motivation to make the combination proposed by the examiner in view of the specific teaching away, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer when expressed in cells as taught by Agami and Sharp.

Claims 1, 5, and 6 are rejected under 35 U.S.C. 103(a) as being unpatentable over either Agami taken with Doglio in further view of either Yu or Ambros as applied to claims 1, 2, and 11-16 above, and further in view of Lorens (US 20040005593).

However, at the time the invention was made, Lorens teaches an RNAi molecule having a loop containing at least 6 nucleotide bases (page 7).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of either Agami taken with either Yu or Ambros and Doglio in further view of Lorens, namely to produce an expression cassette comprising an adenoviral VA promoter, wherein an RNAi molecule comprises a loop containing about 8 nucleotide bases. One of ordinary skill in the art would have been motivated to combine the teaching to increase the inhibition by using a common structure in a shRNA or precursor miRNA molecule to make the expression cassette. See KSR v. Teleflex, Id.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In response to applicant's argument that there is no motivation in the cited art to make such a substitution in the art for a skilled artisan to reasonable expect that the shRNA inserted into the VA1 transcript would be cleaved out, thus making it a substrate for Dicer, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA

transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer when expressed in cells as taught by Agami and Sharp.

In response to applicant's argument that Rossi teach away from the presently claimed subject matter (ribozyme or antisense inserted into VA1 region are not processed out of the VA1 transcript which shRNA must be processed out of the VA1 transcript and cleaved by Dicer in order to be active) and provides no motivation to make the combination proposed by the examiner in view of the specific teaching away, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3). Thus, the transcript would be cleaved and become a substrate for Dicer when expressed in a cell as taught by Agami and Sharp.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, and 11-16 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-9 of U.S. Patent No. US 6,995,258 taken with Agami et al. (US 7,241,618) and Doglio et al. (US 5,837,503) in further view of Zeng et al. Mol. Cell, 9, 1327-33, 2002 and Yu (of record). Claims 1 and 7-9 of '258 recite an expression cassette comprising a coding sequence for an RNA molecule an RNA pol III promoter sequence. One of ordinary skill in the art would understand that to express the RNA molecule in a cell the RNA pol III promoter would have to be operably linked to the RNA molecule. However, the claims from '258 do not specifically teach using a VA1 promoter as the RNA pol III promoter to express RNAi, wherein the RNAi is selected from shRNA or precursor miRNA.

Agami et al. teach making and using an expression cassette comprising an adenoviral VA1 promoter operably linked to an siRNA molecule, wherein the siRNA molecule can be shRNA (columns 50-51 and Figures 8 and 10 and claim 3). Agami et al. teach that siRNA is a substrate for mammalian Dicer (columns 1-3). However, Agami does not specifically teach using RNAi in the vector, wherein the RNAi is precursor miRNA. In addition, Agami does not specifically teach the structural limitations of the VA1 promoter set forth in claims 1 and 2.

However, at the time the invention was made, Doglio et al. teach an expression cassette comprising a DNA oligonucleotide has been inserted between or outside the boxes A and B constituting the promoter of said VA gene or into VA1 gene (columns 8, 10-15, and 19-22).

In addition, at the time the invention was made, Zeng teaches that natural and designed microRNAs (miRNA) can inhibit the expression of mRNAs expressed in human cells (page 1327).

Furthermore, at the time the invention was made, Yu teaches an RNA polymerase III vector comprising shRNA can inhibit expression in mammalian cells.

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '258 taken with Agami and Doglio in further view of either Zeng or Yu, namely to produce an expression cassette comprising an RNAi molecule operably linked to a VA1 promoter, wherein the RNAi is selected from either shRNA or precursor miRNA. One of ordinary skill in the art would have been motivated to combine the teaching to improve the stability of the RNA molecule.

In addition, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the claims of '258 taken with Agami and Doglio in further view of either Zeng or Yu, namely to produce a mammalian cell comprising the expression cassette comprising an RNAi molecule operably linked to a VA1 promoter, wherein the RNAi molecule is selected from either precursor miRNA or

shRNA. One of ordinary skill in the art would have been motivated to combine the teaching to the study the delivery of the siRNA to the nucleolus of the cell.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In response to applicant's argument that there is no motivation in the cited art to make such a substitution in the art for a skilled artisan to reasonable expect that the shRNA inserted into the VA1 transcript would be cleaved out, thus making it a substrate for Dicer, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer as taught by Agami and Sharp.

In response to applicant's argument that Rossi teaches away from the presently claimed subject matter (ribozyme or antisense inserted into VA1 region are not processed out of the VA1 transcript which shRNA must be processed out of the VA1 transcript and cleaved by Dicer in order to be active) and provides no motivation to make the combination proposed by the examiner in view of the specific teaching away, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are

cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer as taught by Agami and Sharp.

Claims 1, 5, and 6 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-9 of U.S. Patent No. US 6,995,258 taken with Agami et al. (US 7,241,618) taken with Doglio et al. (US 5,837,503) in further view of Zeng et al. Mol. Cell, 9, 1327-33, 2002 as being unpatentable over claims 1, 2, and 11-16 in further view of Lorens (of record). Claims 1 and 7-9 of '258 recite an expression cassette comprising a coding sequence for an RNA molecule an RNA pol III promoter sequence. One of ordinary skill in the art would understand that to express the RNA molecule in a cell the RNA pol III promoter would have to be operably linked to the RNA molecule. However, the claims from '258 do not specifically teach using a VA1 promoter as the RNA pol III promoter to express RNAi, wherein the RNAi is selected from shRNA or precursor miRNA.

However, at the time the invention was made, Lorens teaches an RNAi molecule having a loop containing at least 6 nucleotide bases (page 7).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of claims of '258 taken with Agami, Doglio, and either Zeng or Yu in further view of Lorens, namely to produce an expression cassette comprising an adenoviral VA promoter, wherein an RNAi molecule comprises a loop containing about 8 nucleotide bases. One of ordinary skill in the art would have been motivated to combine the teaching to increase the inhibition by using a

common structure in a shRNA or precursor miRNA molecule to make the expression cassette. See KSR v. Teleflex.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In response to applicant's argument that there is no motivation in the cited art to make such a substitution in the art for a skilled artisan to reasonable expect that the shRNA inserted into the VA1 transcript would be cleaved out, thus making it a substrate for Dicer, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the VA1 transcript because the transcript would be cleaved and become a substrate for Dicer as taught by Agami and Sharp.

In response to applicant's argument that Rossi teaches away from the presently claimed subject matter (ribozyme or antisense inserted into VA1 region are not processed out of the VA1 transcript which shRNA must be processed out of the VA1 transcript and cleaved by Dicer in order to be active) and provides no motivation to make the combination proposed by the examiner in view of the specific teaching away, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are

cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the transcript would be cleaved and become a substrate for Dicer as taught by Agami and Sharp.

Claims 1, 2, and 3 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 7-9 of U.S. Patent No. US 6,995,258 taken with Agami et al. (US 7,241,618), Doglio et al. (US 5,837,503) and Zeng et al. Mol. Cell, 9, 1327-33, 2002 or Yu (of record) as being unpatentable over claims 1, 2, and 11-16 in further view of Cagnon (of record). Claims 1 and 7-9 of '258 recite an expression cassette comprising a coding sequence for an RNA molecule an RNA pol III promoter sequence. One of ordinary skill in the art would understand that to express the RNA molecule in a cell the RNA pol III promoter would have to be operably linked to the RNA molecule. However, the claims from '258 do not specifically teach using a VA1 promoter as the RNA pol III promoter to express RNAi, wherein the RNAi is selected from shRNA or precursor miRNA.

However, at the time the invention was made, Cagnon teaches inserting an RNAi molecule into a VA 1 expression cassette using a filled-in Not1 site that was ligated into the BstEII cleaved, filled in vector (page 252).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of claims from '258 taken with Agami and Doglio and either Yu or Zeng in further view of Cagnon, namely to produce the expression cassette wherein the non-essential stem region contains a BstEII site. One of ordinary skill in the art would have been motivated to combine the teaching to

clone the siRNA into the VA1 promoter of the expression cassette since the restriction site is found in an adenoviral VA1 promoter. See KSR v. Teleflex.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

In response to applicant's argument that there is no motivation in the cited art to make such a substitution in the art for a skilled artisan to reasonable expect that the shRNA inserted into the VA1 transcript would be cleaved out, thus making it a substrate for Dicer, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are cleaved (see Agami, columns 1-3 and Sharp, of record). Thus, the RNAi molecule is not required to be cleaved out of the VA1 transcript because the transcript would be cleaved and become a substrate for Dicer as taught by Agami and Sharp.

In response to applicant's argument that Rossi and Cagnon teach away from the presently claimed subject matter (ribozyme or antisense inserted into VA1 region are not processed out of the VA1 transcript which shRNA must be processed out of the VA1 transcript and cleaved by Dicer in order to be active) and provides no motivation to make the combination proposed by the examiner in view of the specific teaching away, the argument is not found persuasive because one of ordinary skill in the art would have been motivated to combine the prior art to successfully express an RNAi molecule in a cell. In addition, one of ordinary skill in the art understands that RNA transcripts are

cleaved (see Agami, columns 1-3). Thus, the transcript would be cleaved and become a substrate for Dicer as taught by Agami and Sharp.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number 571-272-0764. The examiner can normally be reached on from 6:30 to 4:00 (Eastern Standard Time). The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor James Douglas Schultz can be reached on 571-272-0763. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Brian Whiteman/
Primary Examiner, Art Unit 1635